Left Ventricular Dynamics after Aortic Valve Replacement

A Long-term, Combined Radionuclide
Angiographic and Ultrasonographic Study

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*Between January 1985 and July 1990, we studied 71 patients at our institution who
underwent aortic valve replacement for either aortic valve regurgitation (40 patients) or
stenosis (31 patients). The following prostheses were implanted: 25 St. Jude Medical
valves (bileaflet), 16 Björk-Shiley (monoleaflet, tilting disc, 60° convexo-concave), 16
Medtronic-Hall (monoleaflet, tilting disc), and 14 Starr-Edwards (caged ball). The patients
were evaluated pre- and postoperatively by means of gated blood-pool scintigraphy and
Doppler echocardiography. Postoperatively, each patient was studied at 6 months, 1 year,
and then annually. The evaluations focused upon 1) scintigraphically assessed left ven-
tricular performance indicators (end-diastolic and end-systolic volume, as well as resting
and exercise ejection fraction) and 2) Doppler-derived hemodynamic indexes (peak and
mean transvalvular pressure gradient, effective orifice area, regurgitant flow, and systolic
wall stress).*

*Early after aortic valve replacement, 55 (77.5%) of the patients had substantial symp-
tomatic relief, with normal hemodynamic values both at rest and during exercise (New
York Heart Association functional class I or II); another 6 patients (8.5%) maintained their
preoperative status in those classes. Within a year after surgery, a majority of patients
showed a significant reduction in left ventricular dimensions. The patients with preop-
erative aortic valve stenosis had a significantly reduced end-diastolic and end-systolic
volume ($p < 0.05$), a moderately reduced left ventricular mass index ($p < 0.01$), and a sig-
nificantly increased exercise ejection fraction ($p < 0.05$); moreover, in all 31 of these
cases, systolic wall stress returned to normal or lower-than-control values ($p < 0.005$).
The patients with preoperative aortic valve regurgitation had a significant reduction in
end-diastolic and end-systolic volume ($p < 0.005$), diastolic wall stress ($p < 0.005$), and a
significant increase in exercise ejection fraction ($p < 0.01$); however, their left ventricular
mass index was not significantly reduced.*

*Optimal long-term survival was afforded by the St. Jude valve in the small size (21
mm) and the Starr-Edwards valve in the large size (27 mm).*

*This study represents the first reported use of a serial, combined radionuclide and
echocardiographic procedure for the follow-up of patients undergoing aortic valve re-
placement. During the 5½-year follow-up period, this combined technique proved highly
accurate for collecting follow-up data, often complementing or correcting simple ultra-
sound results. This diagnostic approach enabled us to 1) obtain information comparable
to or better than that provided by cardiac catheterization, 2) identify complications early,
3) differentiate between valvular and ventricular failure, and 4) suggest the valve of choice
(not always that with the best hemodynamic performance) in patients with different car-
diac variables. Further research is needed to confirm this study, the results of which could
change many medical and surgical strategies for clinical management of the diseased
aortic valve.* **(Texas Heart Institute Journal 1992;19:97-106)**

Aortic valve replacement (AVR) can significantly improve the New York
Heart Association (NYHA) status and left ventricular function of patients
with symptomatic chronic aortic valve disease. Despite valve replace-
ment, however, the long-term prognosis for these patients is often poor, espe-
cially if marked left ventricular impairment is present before surgery.[1-4] In several
angiographic and echocardiographic reports,[1,5] researchers have described at-
tempts to monitor left ventricular performance after AVR. Invasive techniques have
some drawbacks, however: they are expensive, they cannot be performed seri-

ally, and they are not risk-free. Recently, advances in radionuclide angiography and Doppler echocardiography have allowed investigators to evaluate, both qualitatively and quantitatively, those valvular and ventricular variables that can either confirm the success of AVR or indicate prosthesis dysfunction.[5,6] Once careful noninvasive tests have been performed,[7] left ventricular function can be evaluated by means of real-time hemodynamic studies to determine whether the prosthesis has been correctly selected or, in cases of progressive left ventricular failure, whether the problem is caused by prosthesis dysfunction or underlying myocardial disease. This article describes our use of a combined radionuclide-ultrasound technique to evaluate 71 AVR patients prospectively during a 5½-year period.

Patients and Methods

Study Group

Between January 1985 and July 1990, we evaluated 95 patients who underwent AVR at our institution. The following patients were excluded from the study: 5 who had a combined aortic defect, 11 who underwent a concomitant cardiac surgical procedure, 4 who sustained a perioperative acute myocardial infarction, and 4 who died within a few hours after surgery. The remaining 71 patients constituted our study population, including 42 men and 29 women, aged 18 to 75 years. Forty of the patients had aortic valve regurgitation, and the other 31 had aortic valve stenosis. Table I provides details about the valve prostheses that were implanted: 25 St. Jude Medical valves (bileaflet), 16 Björk-Shiley (monoleaflet, tilt-

TABLE I. Number, Type, and Size of Implanted Prostheses in 71 Patients with Aortic Valve Regurgitation or Stenosis

Valve Type	Valve Size (mm)				Total Valves Implanted
	21	23	25	27	
St. Jude bileaflet	8	10	7	0	25
Björk-Shiley monoleaflet, tilting disc, 60° convexo-concave	0	6	9	1	16
Medtronic-Hall monoleaflet, tilting disc	3	7	4	2	16
Starr-Edwards caged ball	0	0	3	11	14
Totals	11	23	23	14	71

ing disc, 60° convexo-concave), 16 Medtronic-Hall (monoleaflet, tilting disc), and 14 Starr-Edwards (caged ball).

Postoperatively, each patient was placed on a mild warfarin anticoagulation regimen, which was adjusted each month according to the prothrombin time. Ten healthy volunteers served as the control group. In all cases, informed consent was obtained.

Intraoperative and postoperative baseline studies were done with Doppler echocardiography alone. Thereafter, our combined radionuclide-ultrasound technique was used to study each patient at 60 days, 6 months, 1 year, and then annually. The mean duration of follow-up was 56 ± 7 months.

Radionuclide Angiography

Using the technique described by Callahan and associates,[8] the patients' red blood cells were labeled with 30 mCi of technetium-99 (Tc-99m). Imaging was performed with a single-crystal gamma camera (Picker Dyna Mo; Picker International, Inc.; Highland Heights, Ohio, USA), providing a 254-mm-diameter field of view. The camera was equipped with a high-sensitivity parallel-hole collimator oriented in the left anterior oblique (LAO) projection. Processing was accomplished with an ADAC 2800 semiautomated computer system (ADAC; Milpitas, California, USA). The camera was oriented in the 45° LAO position with a 15° caudal tilt. Recording of gamma counts was started after the left ventricular region had been clearly visualized on a preliminary display of the radionuclide ventriculogram. High-temporal-resolution cardiac sequences were constructed in a 64x64-pixel matrix. Counting was triggered by computer-based electrocardiographic gating. To define the frame-by-frame left ventricular region, the counting interval for each cycle was divided into 16 frames. The maximal count density was preset at 220 counts per pixel. Global systolic and diastolic function was analyzed from the "best septal" LAO view, for which 16 frames per cycle were obtained with +5% cycle-length windowing, acquiring 200,000 counts per frame. The left ventricular region of interest was carefully chosen to exclude the left atrium, pulmonary veins, and right ventricle throughout the cardiac cycle. After the background region of interest was chosen, a high-resolution time-activity curve was generated. A beat-rejection algorithm was used during image acquisition to eliminate any beat with premature depolarization (lasting 80% of the average baseline cycle duration during pretest monitoring of sinus rhythm) as well as the subsequent beat with postextrasystolic potentiation. Resting and exercise ejection fractions were determined by computer analysis of the time-activity curves, according to previously reported techniques.[9-12] Cardiac output was assessed by means of thermodilution.

A Swan-Ganz catheter and an arterial line were routinely inserted for supine resting and exercise radionuclide angiography. All patients underwent symptom-limited supine bicycle exercise, beginning at 100 or 200 kg-m/min, with doubling of the workload at 3-minute intervals. After equilibrium-gated cardiac imaging was completed, a lead marker was placed over the left ventricle in the LAO projection, and a 60-second static image was acquired in the anterior projection to determine the left ventricular depth and to correct for photon attenuation in the chest. Blood was taken from the arm opposite that of the Tc-99m injection and was counted for 60 seconds to determine the count rate/sec/mL. On the basis of count rate and left ventricular depth, the counts were converted to milliliters of blood, which allowed direct calculation of left ventricular end-diastolic and end-systolic volumes. Then stroke volume, ejection fraction, and cardiac output were determined.

Doppler Echocardiography

Doppler echocardiography was performed with an Ultramark 8 ATL system (Advanced Technology Laboratories; Bothell, Washington, USA) and a Hewlett-Packard 77020 Ultrasound Image System (Hewlett-Packard; Andover, Massachusetts, USA), both of which provided full 2-dimensional ultrasonic cardiac imaging in the pulsed, continuous-wave, and color-flow Doppler modes. Color-flow imaging was used for follow-up analysis after January of 1986. End-diastolic diameter, end-systolic diameter, and septal thickness were measured in the M-mode by examining the left ventricular chamber at the level of the tips of the mitral valve leaflets, just above the insertion of the chordae tendineae into the papillary muscle. By scanning at the aortic root level, we evaluated prosthetic leaflet excursion and measured the aortic root dimensions. B-Mode echocardiography was used to assess real-time segmental ventricular contractility as well as to calculate the resting and exercise ejection fractions: this step was accomplished in a 4-chamber plane by outlining the endocardial border on a "frozen" end-diastolic and end-systolic frame. The volumes were calculated according to the area-length method; 5 consecutive beats were averaged.

Exercise echocardiography was performed immediately after each patient had completed a treadmill test (Bruce protocol). Left ventricular mass was calculated according to the formula used by Devereux and coworkers:[13]

> Left ventricular mass = 1.04 [(end-systolic diameter + end-diastolic diameter + end-diastolic posterior wall thickness + ventricular septal thickness)³ - (end-systolic diameter + end-diastolic diameter)³] - 14 g

To assess blood flow velocity, we used an independent continuous-wave transducer capable of Doppler scanning only. Recorded blood flow velocities were displayed graphically as spectral tracings. Each patient was evaluated from the apical, the high right and left parasternal, and the suprasternal views. Multiple transducer orientation angles were used to record flow velocities as parallel as possible to the ultrasound beam, occasionally with the guidance of color-flow imaging. The highest velocity (V_{max}) that yielded a high-quality tracing, regardless of the view or the ultrasound beam incidence angle, was used to calculate the peak transvalvular pressure gradient (PG) according to the modified Bernoulli equation[6] $PG = 4(V_{max})^2$. Blood flow across the St. Jude valve was optimally assessed from the apical view; both the left and the right high parasternal views were best for all other prostheses. Optimal alignment with transaortic blood flow was easily accomplished in patients with a mono- or bileaflet prosthesis, but different ultrasound-beam incidence angles were necessary to achieve optimal alignment in patients with a Starr-Edwards prosthesis. When ideal alignment could not be obtained, the peak velocity was corrected with the cosine of the intersecting angle. When blood flow velocity in the left ventricular outflow tract (V_{LVOT}) was greater than 1 m/sec, the modified Bernoulli equation was corrected for that value, $PG = 4(V_{max}^2 - V_{LVOT}^2)$, in order to reduce hyperactivity-induced overestimation.[6] When prosthetic incompetence was detected, the PVRT:LVET ratio (time required to reach peak velocity during the ejection phase–to–left ventricular ejection time) was calculated to correct the modified Bernoulli equation for that value.

The mean transvalvular pressure gradient (MG) was calculated by dividing the displayed graphic spectral tracing of the Doppler signal into 40-msec-long tracts and by averaging the squared measurements according to the following equation:

$$MG = 4(V_1^2 + V_2^2 + V_3^2 + ...V_n^2)/n$$

The effective orifice area (EOA) was determined by using the continuity equation

$$EOA = (A_{LVOT})(V_{LVOT})/V_A$$

where A_{LVOT} (the area of the left ventricular outflow tract) is $\pi(D/2)^2$, and V_A is the aortic flow velocity. The mean value of 5 consecutive B-mode measurements was determined.

Pulsed-Doppler measurements of flow velocity in the left ventricular outflow tract (LVOT) were recorded by placing the sample volume in the body of the left ventricle, advancing it gradually toward the aortic valve until a marked increase in peak velocity was detected, and then withdrawing it slightly.[14] A combined transducer, in which the Doppler func-

tion was integrated with 2-dimensional imaging by means of a time-sharing relay, was used to perform left ventricular chamber mapping. When present, aortic prosthetic regurgitation was measured by means of retrograde flow mapping; the transducer was placed at the cardiac apex, and the pulsed-wave sample volume was placed under the guidance of B-mode imaging. The auditory signal was used to reach an optimal spectral tracing. (Flow reversal in the suprasternal notch was assessed only in cases involving the St. Jude valve.)

Aortic regurgitation was considered mild (1+) if the regurgitant jet was detected just below the valvular plane, moderate (2+ to 3+) if the jet was recorded from the anterior leaflet of the mitral valve up to the level of the papillary muscles, and severe (4+) if the jet was detected between the papillary muscles and the cardiac apex. Pulsed-wave, semiquantitative grading was matched with 1) color-flow assessment of the same jet, which was graded according to the quantitative method suggested by Nanda[15] (jet width/LVOT) and 2) the slope of the continuous-wave Doppler tracing of the retrograde flow (mild, <240 m/sec^2; moderate, 240 to 350 m/sec^2; and severe, >350 m/sec^2). End-systolic wall stress (σ_{aft} in g/cm^2) was calculated according to the method proposed by Mirsky and colleagues:[16]

$$\sigma_{aft} = 1.36 \ P_{es} \ [LD/2h(L+D+h)]_{es}$$

where P_{es} is the end-systolic pressure, and L, D, and h are the long-axis, short-axis, and left ventricular wall thickness, respectively. End-diastolic wall stress (σ_{ed}) was calculated in a similar manner for patients with aortic valve regurgitation.

Interobserver variability was determined for all echocardiographic parameters by having a 2nd investigator remeasure and recalculate the values recorded for the 1st study without knowing the results of the initial reading (overall F = 0.89; p <0.005). The mean ejection fractions assessed by the 2 observers correlated well (F = 0.95; p <0.001). Variability results for the mean pressure gradient were as follows: F = 0.918 and p <0.005. Interobserver differences between 2 Doppler echocardiographic studies (performed on the same day in 35 patients and 1 to 4 days apart in the other 36 patients) showed that 15 of the 71 patients had a ≥5% unit change in mean pressure gradient between the 1st and the 2nd studies. Overall interobserver variability was also calculated for MG, EOA, aortic regurgitation, and σ_{aft} with these results: F = 0.89 and p <0.01.

Statistical Analysis
Linear regression analysis was performed to correlate the prosthetic valve size with either the calculated transvalvular pressure gradient or the recorded regurgitant jet. Ventricular dimensional data were subjected to a statistical multiple regression model and analysis of variance. Multivariate discriminant analysis identified several factors as independent predictors of overall survival (see below). The data analysis was done with an M-24 Olivetti computer system, using the STAT Graphics program.

Results

Four patients (4.2% of the original 95 patients) died perioperatively of cardiac failure. These patients were not included in our study population of 71 patients; therefore, perioperative mortality was not taken into account in summarizing the collected data.

Valvular Hemodynamics
Table I shows the type, size, and number of prostheses implanted. Each type of valve exhibited a unique flow pattern.[6] The St. Jude model had the most central flow and was the most easily assessed by Doppler techniques: the spectral tracing usually peaked early in systole and then decreased markedly in subsequent frames. Compared with the other prostheses, this valve showed a lower mean velocity for the same peak value, suggesting that, except for a mild initial obstruction related to opening of the leaflets, the St. Jude flow pattern resembled that of the native valves (i.e., it provided the best effective orifice area at any given size). Blood flow across valves with a single mobile structure (such as the Medtronic-Hall and Björk-Shiley tilting disc models) was best demonstrated at the major orifice of the valve, and a weaker signal was obtained at the minor orifice.[6,17] Because the best-quality tracing was selected for analysis, the gradient may have been slightly underestimated. The Starr-Edwards valve was the most difficult to assess because of its central occlusive design. The pulsed-wave sample volume or the continuous-wave beam had to be placed along the ball at the sewing ring (with the transducer in the high parasternal or suprasternal window) to obtain an adequate tracing.[6,17,18] Color-flow imaging helped guide the ultrasound beam alongside the central flow axis. Depending on the type of valve, the gradient varied considerably without clinical evidence of dysfunction.[6] The St. Jude valve had the lowest recorded transvalvular gradient,[19] ranging from 7 to 21 mmHg (mean, 15 ± 3.2 mmHg). The Starr-Edwards valve had the highest transvalvular gradient, ranging from 18 to 31 mmHg (mean, 25 ± 4.5 mmHg). The Björk-Shiley and the Medtronic-Hall valves had intermediate pressure gradients. As Khan and colleagues[20] have demonstrated, however, Doppler techniques tend to overestimate the transvalvular gradient of the St. Jude valve; in fact, Doppler estimates of this gradient may even be twice as high as those ob-

tained with catheterization methods. Therefore, our relatively low mean transvalvular pressure gradient established for the St. Jude valve was probably overestimated.

When the transvalvular gradient was correlated with valve size, only a moderate reverse correlation was found (r = -0.54). When size and gradient were compared in the St. Jude valve patients alone, an even weaker reverse correlation (r = -0.39) was found. The 8 21-mm valves implanted did not constitute a large enough group, however, for meaningful conclusions to be drawn. The St. Jude valve provided the most effective orifice area at any given valve size. Khan and colleagues[20] have questioned the continuity equation's ability to assess the true orifice area; despite this uncertainty, however, accuracy of assessment is more likely in the St. Jude valve, because the valve's internal sewing ring nearly matches the area available to blood flow. In contrast, the anatomic and functional areas can differ significantly from each other in the monoleaflet and caged-ball prostheses. Minor aortic regurgitation without hemodynamic consequences (except for 2 patients with low cardiac output) was a common finding in patients with a normally functioning mono- or bileaflet prosthesis[6] (Fig. 1). Of the leaflet prostheses, the Björk-Shiley valve had the best diastolic competence, even in the largest size (27 mm). Regurgitation could not always be localized to the valve or to the para-valvular area; eccentricity of the color-flow regurgitant jet, best assessed from the parasternal short-axis view, was usually a marker for paraprosthetic regurgitation. There was a direct correlation between regurgitation grade and valve size (r = 0.83).

Ventricular Findings

Radionuclide ventriculography showed a significant reduction in left ventricular dimensions soon after AVR, whether for aortic valve stenosis or regurgitation, and a corresponding improvement in resting and exercise ventricular performance as well as in NYHA functional class status. Patients with aortic valve stenosis showed a significantly reduced end-diastolic and end-systolic volume (p <0.05), a moderately reduced left ventricular mass index (p <0.01), and a significantly increased exercise ejection fraction (p <0.05). Moreover, their end-systolic wall stress returned to normal or lower-than-control values. Patients with aortic valve regurgitation had a significantly reduced end-diastolic and end-systolic volume (p <0.005) and diastolic wall stress (p <0.005); but their left ventricular mass index did not decrease significantly, and no important changes were observed in their postoperative ejection fraction at rest. On the other hand, these patients had a significantly increased exercise ejection fraction (p <0.05) (Table II).
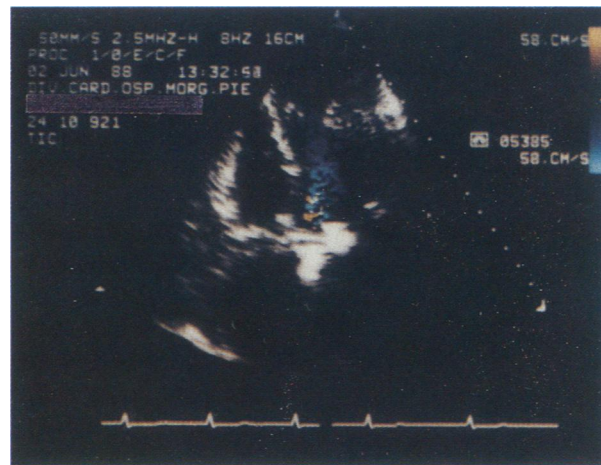

Fig. 1 Color-flow Doppler image of a 27-mm Medtronic-Hall monoleaflet valve shows regurgitant jet across the valve in the apical 5-chamber view. Despite this evidence, no negative hemodynamic consequences were found.

Within 6 months after surgery, 61 (86%) of the patients were in NYHA functional class I or II: 55 (77.5%) had improved by 2 or more NYHA classes and another 6 (8.5%) maintained their preoperative status in class I or II (Fig. 2). In patients with preoperative aortic valve regurgitation, the mean reduction in end-diastolic diameter was 1.1 ± 0.7 cm after 6 months, 1.5 ± 0.3 cm after 1 year, and 1.6 ± 0.6 cm after 2 years (Figs. 3 and 4); in these same patients, the mean reduction in end-systolic diameter was 1.0 ± 0.8 cm after 6 months, 1.3 ± 0.4 cm after 1 year, and 1.34 ± 0.3 cm after 2 years (Fig. 5).

Multivariate discriminant analysis indicated that age, preoperative NYHA class, and a diagnosis of aortic valve regurgitation were independent predictors of overall survival, but valve size was not. In

TABLE II. Mean Resting and Exercise Ejection Fractions for 71 Aortic Valve Regurgitation and Stenosis Patients

Diagnosis	Preop	Postop
Aortic stenosis (n=31)		
Mean resting EF (%)	64 ± 2	65 ± 7
Mean exercise EF (%)*	66 ± 8	74 ± 3
Aortic regurgitation (n=40)		
Mean resting EF (%)	58 ± 3	62 ± 2
Mean exercise EF (%)*	59 ± 4	68 ± 5

EF = ejection fraction

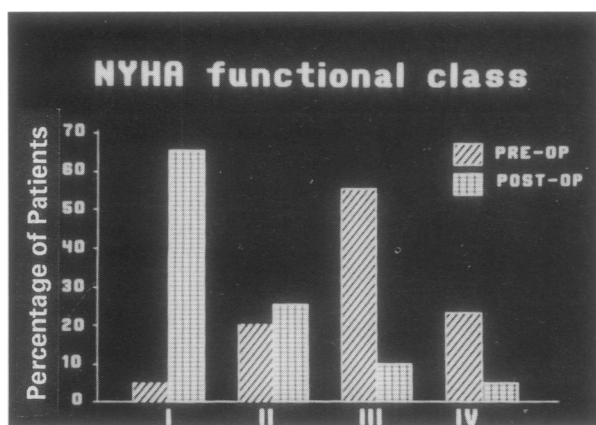* Pre- and postoperative differences statistically significant (p <0.05)

Fig. 2 Preoperative and postoperative NYHA functional class: preoperatively, 6 (8.5%) of the patients were in NYHA class I or II; postoperatively, 61 (86%) were in these 2 classes.
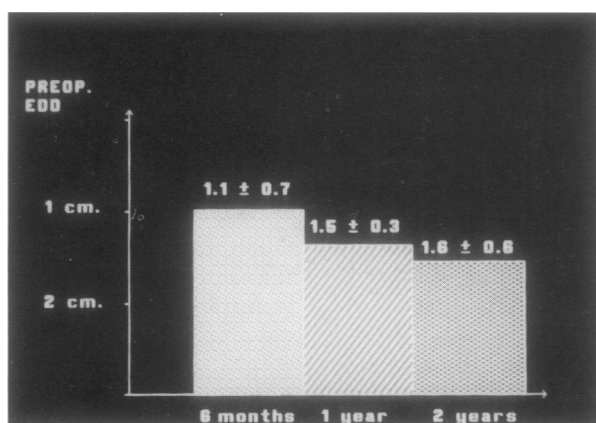
NYHA = New York Heart Association

Fig. 4 The end-diastolic diameter (EDD) reduction data for the aortic regurgitation patients, obtained at 6-month follow-up, were analyzed statistically. This scatterplot shows results of the multiple regression analysis. Significant variability was found. Analysis of the variance showed a significant statistical difference between the preoperative EDD and the EDD at 1-year follow-up (F = 10.66; p = 0.0085; df = 3; confidence intervals = 95%).

EDD = end-diastolic diameter

Fig. 3 Mean reduction in end-diastolic diameter is shown 6 months, 1 year, and 2 years after aortic valve replacement for aortic regurgitation.

EDD = end-diastolic diameter
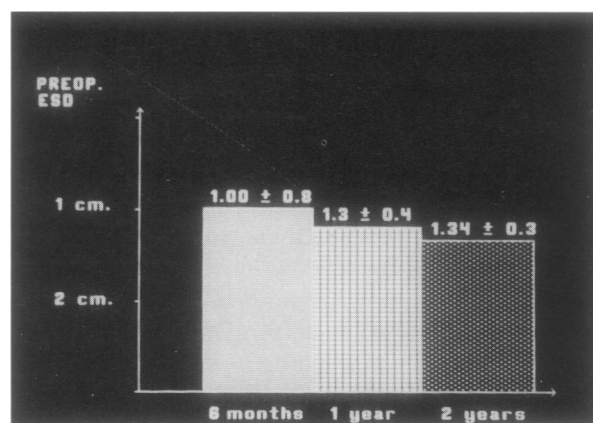
Fig. 5 Mean reduction in end-systolic diameter is shown 6 months, 1 year, and 2 years after aortic valve replacement for aortic regurgitation.

ESD = end-systolic diameter

patients with a small prosthesis (21 mm), the mean transvalvular pressure gradient never exceeded 20 mmHg, and satisfactory ventricular recovery was possible. The small Starr-Edwards prostheses could not be implanted because of their tendency to be too occlusive (i.e., residual systolic overload >50 mmHg).[4,19] Most often, the 21-mm St. Jude and Medtronic-Hall prostheses were implanted in the aortic stenosis patients, in women, and in elderly patients. Perioperative mortality, postoperative mortality, and NYHA status all seemed to be unaffected by prosthesis size.[21] Of the 11 patients receiving a small prosthesis (8 St. Jude and 3 Medtronic-Hall valves), 8 improved by 2 or more NYHA classes (from class III or IV to class I); 1 improved from class IV to class II and 1 from class III to II. In the 11th patient (with a 21-mm Medtronic-Hall valve), early improvement
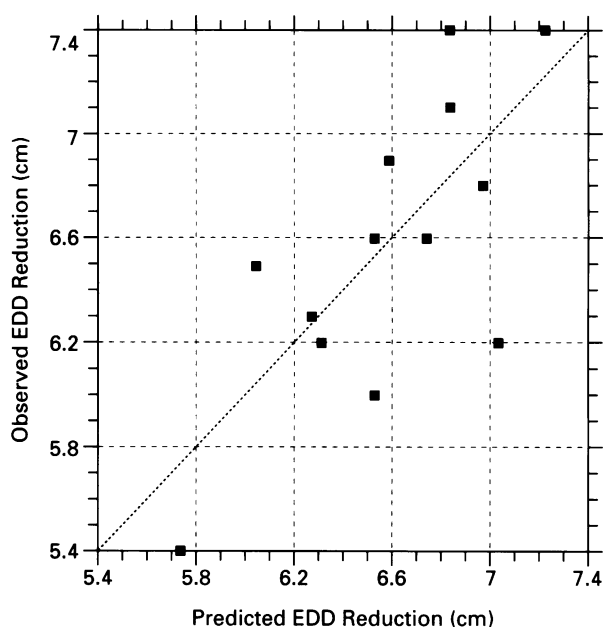
was followed by a transient ischemic attack 1 year postoperatively; 4 years later, reoperation was performed for prosthesis-related thrombosis.

Reoperation

Reoperation was necessary in 5 patients; all were severely symptomatic (NYHA class III or IV), and 4

had severe prosthetic dysfunction, as quantitated by Doppler echocardiography. The mean time between surgical implantation and Doppler-detected prosthetic dysfunction was approximately 5 years. Thrombosis occurred in 2 patients (1 who had a 21-mm Medtronic-Hall valve and the other, a 25-mm Björk-Shiley valve). Dehiscence secondary to subacute infective endocarditis occurred in 2 patients (involving a 25-mm Björk-Shiley and a 27-mm Starr-Edwards valve). The 5th patient (with a 25-mm St. Jude valve) who underwent reoperation manifested no evidence of prosthetic dysfunction, showing moderate left ventricular improvement early after surgery, but developing severe left ventricular enlargement 3 years after surgery (end-diastolic diameter, 7.8 cm; end-systolic diameter, 6.3 cm) with neither clinical nor Doppler evidence of valve dysfunction. This 33-year-old patient is scheduled to undergo cardiac transplantation for probable primary myocardial disease. Reoperation was successful in all patients.

Thromboembolism

Two thromboembolic events occurred during the follow-up period: 1 patient, mentioned above, who had a 21-mm Medtronic-Hall valve and a prothrombin time of 30%, suffered a transient ischemic attack a year after surgery and underwent reoperation 4 years later for massive prosthesis-related thrombosis. The other patient, who had a 25-mm Björk-Shiley valve and a prothrombin time of 34%, also underwent reoperation (31 months after surgery) and died of stroke 26 months later. No major anticoagulation-related hemorrhage was reported.

Mortality

Eight cardiac-related deaths occurred during the follow-up period, for a linear overall mortality rate of 11%. One patient, mentioned above, died of a stroke, of probable cardiac origin, 26 months after reoperation. Three patients with leaflet prostheses died suddenly, possibly of acute valve obstruction:[17] 1 patient, who had a 23-mm Medtronic-Hall valve, died 3 years after surgery; the other 2 patients, 1 with a 23-mm and the other a 25-mm Björk-Shiley prosthesis, died 4 and 5 years (respectively) after surgery. In all 3 of these cases, the most recent serial Doppler study had shown no evidence of prosthetic dysfunction or left ventricular impairment, and death was preceded by no symptoms. Autopsy revealed massive prosthetic thrombosis in 2 of the patients but did not confirm suspected acute valvular failure in the 3rd.

One man (Table III) and 1 woman (Table IV) died of irreversible progressive heart failure culminating in cardiogenic shock (10 and 20 months after AVR, respectively); both were elderly (71 and 75 years of age) and had low preoperative cardiac output. Im-

TABLE III. Progressive Heart Failure in a 71-Year-Old Man* with a 27-mm St. Jude Valve and Low Preoperative Cardiac Output

Variables	Preop	After 6 Months
Valvular indexes		
Mean gradient (mmHg)	28	11
Peak gradient (mmHg)	56	27
NYHA functional class	IV	III to IV
Degree of regurgitation	3+ to 4+	1+ to 2+**
Ventricular indexes		
End-diastolic diameter (cm)	8.2	8.2
End-systolic diameter (cm)	6.6	6.6
Shortening fraction	19%	19%
Septal thickness (cm)	1.0	1.0

NYHA = New York Heart Association

* No improvement in left ventricular performance or NYHA class was observed after surgery. Further progressive left ventricular deterioration occurred, and the patient died 10 months postoperatively.
** Approximated from catheterization studies.

TABLE IV. Progressive Heart Failure in a 75-Year-Old Woman* with a 25-mm St. Jude Valve and Low Preoperative Cardiac Output

Variables	Preop	After 6 Months	After 1 Year
Valvular Indexes			
Mean gradient (mmHg)	—	9	9
Peak gradient (mmHg)	—	21	21
NYHA functional class	III	III	IV
Degree of regurgitation	3+ to 4+	1+ to 2+**	1+ to 2+**
Ventricular Indexes			
End-diastolic diameter (cm)	7.0	7.1	7.4
End-systolic diameter (cm)	4.8	5.2	5.6
Shortening fraction	30%	26%	24%
Septal thickness (cm)	1.0	0.9	0.8

NYHA = New York Heart Association

* Neither left ventricular performance nor NYHA class improved after surgery; the patient died 20 months postoperatively of cardiogenic shock. Because of her age and the severity of left ventricular impairment, reoperation was not attempted.
** Approximated from catheterization studies.

plantation of the larger St. Jude valves (27 and 25 mm, respectively) in these patients may have been inappropriate, because both valves proved moderately incompetent soon after surgery.

Two other patients with severely impaired preoperative left ventricular performance experienced postoperative subacute cardiac failure (Table V). These patients were operated upon because of their young age (45 and 55 years) and their otherwise poor prognosis.

Discussion

Equilibrium-gated radionuclide ventriculography confirmed that left ventricular dimensions returned to nearly normal within 1 to 2 years after successful AVR, the most significant reduction occurring within the 1st 6 months. The surgical procedure involved an acceptable perioperative and intermediate-term mortality.[21] Eighty-six percent of the patients were in NYHA functional class I or II postoperatively, either having improved by 2 or more classes (77.5%) or having maintained their preoperative status (8.5%). Thus, AVR was highly successful in treating aortic valve disease (in accord with the findings of others)[2,5]. Despite an excellent early prognosis (usually up to 5 years after surgery) and better survival than if the primary disorder had remained untreated, late results were less satisfactory because of an increased incidence of prosthetic dysfunction, reoperation, thromboembolic events, and sudden death. Moreover, compared with normal native valves, all available prosthetic aortic valves are relatively stenotic; therefore, when such valves are used, the effects of

TABLE V. Impaired Preoperative Left Ventricular Performance in 2 Patients with Postoperative Subacute Cardiac Failure

Variables	Patient #1	Patient #2
Age (years)	45	55
End-diastolic diameter (cm)	7.7	7.8
End-systolic diameter (cm)	7.0	6.3
Shortening fraction	10%	19%
Septal thickness (cm)	0.9	1.0
End-diastolic wall stress* (g/cm²)	75	70

* The value of end-diastolic wall stress in both patients is highly indicative of increased compensatory activity of the preload on ejection fraction (Masotti; unpublished observation, 1992). That compensatory activity could be reduced by surgery, with a subsequent negative outcome.

unavoidable chronic excess afterload are superimposed upon the long-term sequelae of the preexisting hemodynamic overload.[2] This fact is of substantial concern, because many patients who require AVR are relatively young and would otherwise have a long life expectancy.[2] The size of the valve, and hence, the size of the aortic root is a main determinant of residual overload. Typically, residual overload is a function of valve pathology (aortic stenosis), which is, in turn, often a function of the patient's age (relatively young) and is often related to the patient's sex (male) and diagnosis.

The Starr-Edwards prosthesis is too occlusive to be inserted into a small (<25 mm) aortic root;[4,19] but when the aortic root is large enough to permit its implantation, the Starr-Edwards valve provides the best long-term survival, with a very low incidence of complications and sudden death. Management of the small aortic root may necessitate an annuloplasty, followed by implantation of a monoleaflet (or better, a bileaflet) valve to prevent excessive residual afterload. In our series, AVR with a small, leaflet prosthesis resulted in excellent symptomatic improvement. We observed no correlation between valve size and overall survival or NYHA functional class improvement. The reverse correlation between valve size and pressure gradient appeared comparatively weak in the case of the St. Jude prosthesis, suggesting that even small St. Jude valves offer optimal hemodynamic performance. (This finding may conflict with previous experiences;[22] nevertheless, this correlation was carefully evaluated, despite the small number of St. Jude valves used in our series.)

Unfortunately, in patients with a low cardiac output, bileaflet valves (especially St. Jude models >23 mm) allow an amount of regurgitant flow that, although negligible under basal conditions, can seriously affect the regurgitant fraction (and thus, the forward as well as the retrograde flow) if myocardial depression develops.[23] Residual volume overload may negatively affect a technically successful surgical outcome, as in 2 of our patients (Tables III and IV). In fact, one of the most serious challenges in the surgical management of diseased aortic valves involves the decision to perform AVR in patients with severe left ventricular impairment.[1,3] As 4 of our cases showed, such patients have a 50% risk of postoperative subacute cardiac failure or persistent cardiomegaly. Although the proximate cause of these problems seems related to surgically induced impairment of the compensatory preload mechanism in the failing left ventricular myocardium,*[16,24] the underlying cause is the preexisting myocardial damage. It is not yet known why, after AVR, 50% of these patients have a significant reduction in ventricular dimen-

*Masotti and colleagues. Unpublished observation, 1992.

sions and experience symptomatic improvement.[4] In an angiographic study, however, Monrad and associates[2] reported that during the 1st 6 postoperative months, patients with aortic valve regurgitation and severe left ventricular dysfunction returned to normal hemodynamics at rest but not during exercise. Thus, even though the majority of patients experience improved postoperative left ventricular function at rest, they may never regain their normal ventricular performance throughout the full range of physiologic demand. This lack of full ventricular performance may be demonstrated either by a reduced increase in the ejection fraction and an abnormal increase in the pulmonary capillary wedge pressure during exercise radionuclide ventriculography (as in 4 of our patients) or by the latter indication alone. If the myocardial depression has lasted for more than a year, careful diagnostic evaluation is mandatory before AVR is undertaken. In selected patients, an alternative such as elective cardiac transplantation should be considered.

In this study, we found persistent myocardial hypertrophy and systolic hyperfunction late after AVR, indicating that, unlike the preload response (Frank-Starling mechanism), the hypertrophic response of an overloaded ventricle does not abate when the hemodynamic imbalance is eliminated. Further investigations are warranted to determine the meaning of these contrasting responses. The patients in our study also showed diminished end-systolic wall stress late after surgery (a lower afterload per unit of myocardium) in comparison with controls (see Ventricular Findings). Together, persistent hypertrophy and reduced end-systolic stress may explain the increased left ventricular ejection fraction commonly encountered in our late follow-up analyses.

Conclusions

Despite more than 20 years of experience with over 50 cardiac valve prostheses, surgeons are still seeking an ideal replacement valve. In our experience, the valve with the best hemodynamic profile (the St. Jude) was not always the valve of choice: for instance, in the case of a patient with a large aortic root and low cardiac output. Moreover, this valve did not always result in the best long-term survival: when a 27-mm valve was required, the Starr-Edwards model seemed to provide the best survival. Further investigations involving more patients are needed to confirm these findings.

Nevertheless, implantation of a St. Jude valve is contraindicated only in a limited number of patients. Most patients can take advantage of this valve's nearly ideal features, including its satisfactory hemodynamic characteristics and low thrombogenicity

(which resembles that of bioprosthetic valves, allowing administration of lower doses of warfarin than those necessary with other mechanical valves).[25] Other advantages include durability, structural integrity, ease of insertion, lack of hemolysis, and absence of noise. Therefore, we believe that, in the absence of the contraindications discussed above, the St. Jude valve is the prosthesis of choice for the surgical treatment of chronic aortic valve disease.

This study represents the first reported use of a serial, combined radionuclide and echocardiographic procedure for follow-up of patients with aortic valve replacement. During the $5\frac{1}{2}$-year follow-up period, this combined technique proved highly accurate for collecting follow-up data, often complementing or correcting simple ultrasound results. This diagnostic approach enabled us to 1) obtain information comparable to or better than that provided by cardiac catheterization, 2) identify complications early, 3) differentiate between valvular and ventricular failure, and 4) suggest the valve of choice (not always that with the best hemodynamic performance) for different cardiac situations. If confirmed by other studies, these data could change many medical and surgical strategies for the clinical management of the diseased aortic valve.

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